REMARKS

Claims 1-5, 7-17, 19-25, and 27-34 were pending. Claims 4, 16, 29, 30, and 32-34 are withdrawn. Applicants have amended claims 1, 2, 5, 7, 9, 10, 13, 17, 27, 30, and 33 and the specification paragraph starting at page 1, line 25. Support for the claim and specification amendments may be found in the claims and specification as filed. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

Statement of Substance of Telephone Interviews

At the outset, Applicants thank the Examiner for the courtesies extended during the telephone interviews conducted on February 27, 2009 and March 18, 2009. During the initial interview, the Examiner and Applicants' representatives discussed the rejection of the claims under 35 USC 101, which rejection is addressed further below.

Claim Rejections – 35 U.S.C. § 101

Claims 1-3, 5, 7-15, 17, 19-25, 27, 28, and 31 are rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory subject matter. Applicant respectfully traverses the rejection for the reasons that follow.

Independent claim 1 is directed to "a cDNA microarray data correction system," as amended. The system of claim 1 comprises among other elements "a data standardization unit within a data analyzer processor for standardizing the gene expression intensity data," "a spot-based correction unit within a data analyzer processor configured to estimate a distortion depending on a spot position within a one of the plurality of grids for the standardized gene expression intensity data," and "a Sum-Difference (S-D) plot based correction unit within a data analyzer processor configured to perform a Sum-Difference (S-D) transformation for the first corrected gene expression intensity data."

Independent claim 13 is directed to "a cDNA microarray data correction method [] performed within a cDNA microarray data correction system," as amended. The method of claim 13 comprises among other steps "standardizing by a data standardization unit within a data analyzer processor the gene expression intensity data," "estimating by a spot-based

correction unit within a data analyzer processor a distortion depending on the spot position within a one of the plurality of grids for the standardized gene expression," and "performing by a Sum-Difference (S-D) plot based correction unit within a data analyzer processor a Sum-Difference (S-D) transformation for the first corrected gene expression intensity data."

Lastly, independent claim 27 is directed to "a computer-readable memory medium containing a cDNA microarray data correction program for use in correcting global and local distortions of microarray data [] with a cDNA microarray data correction system," as amended. The program contained in the computer-readable medium of claim 27 when executed performs among other steps "standardizing by a data standardization unit within a data analyzer processor the gene expression intensity data," "estimating by a spot-based correction unit within a data analyzer processor a distortion depending on the spot position within a one of the plurality of grids for the standardized gene expression," and "performing by a Sum-Difference (S-D) plot based correction unit within a data analyzer processor a Sum-Difference (S-D) transformation for the first corrected gene expression intensity data."

Applicants note that the feature of "to a display device" has been removed from each of independent claims 1, 13, and 27. Applicants acknowledge the broadening amendment, but do not believe the recitation is necessary for patentability.

In the Office Action, the Examiner cites *In re Bilski* in the rejection of each of independent claims 1, 13, and 27. As an initial matter, Applicants do not agree that *Bilski* is applicable to claim 1 or claim 27, as amended. The Office Action acknowledges that *Bilski* is only applicable to the determination of whether a "process" is patent eligible. Office Action, at page 3. That is, independent claim 1 is directed to a "system," while independent claim 27 is directed to a "computer-readable memory medium." Therefore *Bilski* is inapplicable to claim 1 and claim 27. However, in response to the rejection, Applicants respectfully traverse the § 101 rejection in light of the amended independent claims for the reasons that follow.

According to the Court in *Bilski* the relevant questions are whether: (1) the claimed process is tied to a *particular machine* or *apparatus*; or (2) the claimed process transforms a *particular article* into a *different state* or *thing*. 2007-1130, at 10 (en banc) (Fed. Cir. October

30, 2008). While the plain language of this test appears simple to apply, the Federal Circuit also provided context to the test through "a wealth of detailed guidance and helpful examples on how to determine the patent eligibility of process claims." *Id.* at 18.

Taking the second prong first, each of the independent claims satisfy the *Bilski* test. That is, under the broadest possible construction independent claims 1, 13, and 27 require the use of a machine or apparatus. In other words, none of claims 1, 13, and 27 can be performed by a human alone. As such, these claims as amended do not attempt to "wholly preempt an abstract process."

Among other limitations, an input device, a data analyzer processor, and an output device are recited in claim 1 as amended. Clearly, at least the input device, data analyzer processor, and the output device are components of a machine. Each of the claim features recite at least one of these components, including those limitations directed at transformation of "gene intensity data." That is, each of the units within the data analyzer processor are involved in transformation of data beyond gathering and outputting. Accordingly, the claimed system is at least tied to an input device, a data analyzer processor, and an output device and therefore satisfies the requirements of § 101.

Similarly, claim 13 as amended is a method "performed within a cDNA microarray data correction system." Each of the method steps directed at transformation of "gene intensity data" recite such transformation as being accomplished by units within a data analyzer processor. Accordingly, the recitation of the particular machine of a "data analyzer processor" satisfies the machine prong of the test such that claim 13 satisfies the requirements of § 101. That is, the claim 13 method steps directed to activity other than gathering or outputting data recite the particular machine of "data analyzer processor."

Lastly, claim 27 is directed to a "computer readable memory medium" and also recites the limitation of "a cDNA microarray data correction system." Similar to claim 13, claim 27 recites the particular machine of "a data analyzer processor" in those features directed at transformation of "gene intensity data." Accordingly, claim 27 satisfies the machine prong of the machine-transformation test and satisfies the requirements of § 101.

Further, each of claims 1, 13, and 27 satisfy the first transformation prong of the test. More specifically, these claims are directed to transforming "gene intensity data" into another state ultimately for transmission and display. Each of the claims include features directed to "standardizing the gene intensity data," "estimating a distortion for the standardized gene intensity data," and "performing a Sum-Difference (S-D) transformation for the first corrected gene expression intensity data." The gene expression intensity data "clearly represent[s] physical and tangible objects," namely the data represents the expression of collections of genes. Accordingly, Applicants submit that the Examiner's assertion that "[t]he instant claims do not recite or inherently involve any transformation of a particular article" as contemplated by the *Bilski* transformation prong is incorrect.

Further, Applicants direct the Examiner's attention to the discussion of *In re Abele*, which the *Bilski* opinion describes to "gain insight into the transformation part of the test." *Id.* at 25 (discussing *In re Abele*, 684 F.2d 902 (CCPA 1982)). In particular, the Federal Circuit's discussion of *Abele* was for the purpose of explaining the "boundaries of what constitutes patent-eligible transformation of articles." *Id.* at 25. More particularly, the claims at issue in *Abele* were as follows:

> 5. A method of displaying data in a field comprising the steps of:
>
> calculating the difference between the local value of the data at a data point in the field and the average value of the data in a region of the field which surrounds said point for each point in said field, and
>
> displaying the value of said difference as a signed gray scale at a point in a picture which corresponds to said data point.
>
> 6. The method of claim 5 **wherein said data is X-ray attenuation data produced in a two dimensional field by a computed tomography scanner**.

The Federal Circuit in *Bilski* stated claim 5 was held unpatentable because "[t]hat claim did not specify any particular type or nature of data: nor did it specify how or from where the data was obtained or what the data represented." *Id.* at 25. In contrast, claim 6 was held patentable as directed to patentable subject matter "where it specified that 'said data is

X-ray attenuation data produced in a two dimensional field by a computed tomography scanner'" *Id.* at 26. According to the Federal Circuit "[t]his data clearly represented physical and tangible objects, namely the structure of bones, organs, and other body tissues. Thus, the transformation of that raw data into a particular visual depiction of a physical object on a display was sufficient to render that more narrowly-claimed process patent-eligible." *Id.* at 26. Additionally, the Federal Circuit "further note[d] for clarity that the electronic transformation of the data itself into a visual depiction in *Abele* was sufficient; the claim was not required to involve any transformation of the underlying physical object that the data represented." *Id.* at 26.

Similarly, the features of pending claims 1, 13, and 27 are directed to transformation of data that clearly represents the physical and tangible objects of collections of genes for transmission and display. These claims are therefore transformative for the same reasons as claims 6 as set forth in *Abele*. Applicants note that during the first telephone interview held on February 27, 2009 the Examiner posited the position that one would have difficulty finding any situation in which data transformed within a claim did not somehow represent something "in the real world." However, Applicants respectfully disagree that such a position forecloses satisfaction of the first prong of the *Bilski* test, particularly with claims 1, 13, and 27 that clearly recite transformation of data that represents physical and tangible objects. The assertion of the Examiner's posited position would render the Federal Circuit's express discussion of *In re Abele* as "insight into the transformation part of the test" meaningless.

Additionally, the Examiner directed Applicants' representatives attention to the non-precedential Board of Patent Appeals and Interferences decision of *Ex parte Marius A. Cornea-Hasegan*. Appeal 2008-4742 (BPAI January 13, 2009). Applicants thank the Examiner for identifying the board decision as potentially relevant while not binding, and respectfully submit that the claims at issue in *Cornea-Hasegan* are distinguishable from Applicants pending claims for a host of reasons.

At the outset, Applicants note that the claims in *Cornea-Hasegan* merely recited a generic processor. *See Cornea-Hasegan* at 2-3 (recitation of claims 1 and 18). In contrast, each of claims 1, 13, and 27 recite a "data analyzer processor." Further, each of these claims

also recite particular "units" within a "data analyzer processor." Such a "data analyzer processor" is a particular machine programmed for the purpose of cDNA microarray data correction. Accordingly, Applicants submit that the recitation of this particular form of a processor is a particular machine that satisfies the machine prong of the *Bilski* test.

Additionally, the scope of the claims at issue in *Cornea-Hasegan* is fundamentally different from the scope covered by the pending independent claims. Applicants note that the *Cornea-Hasegan* claims are directed to a method and a computer readable media comprising steps for predicting results of floating point mathematical operations and calculating the results. *See Cornea-Hasegan* at 2-3 (recitation of claims 1 and 18). In contrast, and as discussed in detail above, claims 1, 13, and 27 are directed to transformation of gene intensity data which clearly represents physical and tangible objects. As such, the claims standing alone, without recitation of the "data analyzer processor," are patentable as satisfying the first transformation prong of *Bilski*.

In contrast, the *Cornea-Hasegan* claims standing alone recite nothing more than mathematical calculations on floating point numbers. Accordingly, the BPAI concluded that allowing patentability by the recitation of merely a generic "processor" would "exalt form over substance and would allow pre-emption of the fundamental principle present in the non-machine implemented method." *Cornea-Hasegan* at 10. The pending claims would not allow pre-emption of a fundamental principle as they are directed to cDNA microarray data correction using a variety of different mathematical transformations and manipulations while the *Cornea-Hasegan* claims are directed to a single algorithm. In simpler terms, unlike the generic processor recitation in the *Cornea-Hasegan* claims, the recitation of a "data analyzer processor" in claims 1, 13, and 27 does not merely exalt form over substance because claims 1, 13, and 27 by their features are substantively transformative.

In sum, the present claims do not "pre-empt the use of a fundamental principle" but rather are drawn to particular applications of mathematical transformations and manipulations for cDNA microarray data correction. *See Cornea-Hasegan* at 8 (quoting *Diehr*, 450 U.S. 175, 187 (1981)). Accordingly, for the reasons set forth above, Applicants respectfully request that the rejection to independent claims 1, 13, and 27 be withdrawn. Moreover,

claims 2-3, 5, 7-12, 14-15, 17, 19-25, 28, and 31 depend from one of claims 1 and 13 and should be allowed for at least the reasons set forth above as well as further patentable limitations cited therein.

Claim Rejections under 35 U.S.C. § 112

Claims 1-3, 5, and 7-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention claimed. Applicants thank the Examiner for withdrawing the previous indefinite and antecedent basis rejections in view of the previously filed amendments. In response, Applicants have amended claims 1, 2, 5, 7, 9, and 10 and respectfully traverse the rejection as follows.

Applicants have amended the claim features of claim 1 to recite "a data standardization unit," "a spot-based correction unit," and "a Sum-Difference (S-D) plot based correction unit." Further, Applicants have amended claim 2 to recite "a Sum-Difference S-D transformation unit." Claims 5, 7, 9, and 10 which depend from independent claim 1 have been similarly amended. Applicants submit that the presented claims as amended are sufficiently supported by the specification of the present application. Accordingly, Applicants respectfully request that the rejection to claims 1 and 2 be withdrawn. Moreover, claims 3, 5, 7-12 depend from claim 1 and are therefore similarly supported such that the rejection should be withdrawn.

Claim Rejections under 35 U.S.C. § 103

Claims 1, 2, 13-14, and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nucleic Acids Research, 2002, Vol. 30, pages 1-10 ("Yang") in view of U.S. Pat. Pub. 2003/0226098 ("Weng"). Applicants respectfully traverse the rejections for the reasons that follow.

Applicants rely on MPEP § 2143 which requires that all the claim limitations be considered. Considering all the claim limitations, as required by MPEP § 2143.03, the cited references do not disclose, teach or suggest all the claim limitations of independent claims 1, 13, and 27 as amended. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

As discussed previously, each of independent claims 1, 13, and 27 are directed to a "system," "method," and "computer-readable memory medium." Independent claim 1 recites, in combination with other features a "spot-based correction unit within a data analyzer processor configured to estimate a distortion depending on a spot position within a one of the plurality of grids," as well as "a Sum-Difference (S-D) plot based correction unit within a data analyzer processor configured to perform a Sum-Difference (S-D) transformation for the first corrected gene expression intensity data."

The purpose of the claimed features is to provide "standardization [] by combining standardization using order statistics over the grids (global standardization) and the correction of a distortion depending on the spot position within a grid (local standardization). Thereby, it becomes possible to correct a systematic error caused by deviation of the gene expression intensities among the grids and a distortion depending on the spot position within an individual grid at a time." Present Application, Page 13, Lines 14-22. Accordingly, the present invention as claimed is able to "simultaneously correct a systematic error caused by deviation of the gene expression intensities among grids or by fluctuations of sensitivity and a distortion depending on the spot position within a grid." Present Application, Page 17, Lines 4-8. While Yang discloses various normalization techniques for use in cDNA microarray experiments, none of the normalization techniques disclosed teach, disclose, or suggest any of these features. More particularly, Yang is directed to correction of distortion only at every grid. Weng does not cure the deficiencies of Yang.

The Office Action asserts "'Scale normalization' section in column 1 (line 8) of page 3 of Yang et al. teaches such a normalization. The equations in this section illustrate a nonparametric smoothing method," in reference to the feature of "spot-based correction unit within a data analyzer processor configured to estimate a distortion depending on a spot position within a one of the plurality of grids," as amended. Office Action, at page 8. However, Applicants submit that the identified "Scale normalization" of Yang does not estimate "a distortion depending on a spot position." Rather, the "Scale normalization" normalizes the data using data about individual spots within a grid (or print tip group). More specifically, Yang discloses the following formulas for "Scale normalization":

$$a_i^2 = (\sum^{n\,i}_{j=1} M_{ij}^2) / [\sqrt[I]{\prod_{k=1}^{I} \sum^{n\,k}_{j=1} M_{kj}^2}]$$

Where M_{ij} denotes the *j*th log ratio in the *i*th print tip group, $j=1, \ldots, n_i$.

and

$$a_i^2 = (MAD_i) / [\sqrt[I]{\prod_{i=1}^{I} MAD_i}]$$

Where the median absolute deviation *MAD* is defined by

$$MAD_i = \text{median}_j\{| M_{ij} - \text{median}_j(M_{ij}) |\}$$

Indeed, as the name suggests, "Scale normalization" is performed by "the scale factors a_i for the different print tip groups [being] estimated then eliminated."

Additionally, the Office Action asserts and Applicants agree that Yang does not teach "Sum Difference (S-D) transformations." However, the citation of Weng does not cure this deficiency of Yang. More particularly, claim 1 recites "a Sum-Difference (S-D) plot based correction unit within a data analyzer processor configured to perform a Sum-Difference (S-D) transformation for the first corrected gene expression intensity data." By way of example, the Examiner's attention is directed to an embodiment illustrated by Figure 9, specifically the X and Y axis therein, as well as the associated discussion of Figure 9 from the Present Application. Present Application, Page 15, Lines 17-20 ("Referring to FIG. 9, there is shown an S-D plot of the distortion. The abscissa indicates a sum of the gene expression intensities of the channels and the ordinate indicates a difference between them."). The "S-D (second derivative) transformation" identified by the Examiner is not a "Sum Difference (S-D) transformation," as claimed.

Accordingly, independent claims 1, 13, and 27 should be allowed for at least the reasons cited above. Moreover, claims 2 and 14 depend from one of independent claims 1 and 13 and should be allowed for at least the reasons recited above as well as for further patentable limitations cited therein.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 4/1/2006 By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 945-6014
Facsimile: (202) 672-5399

George C. Beck
Attorney for Applicant
Registration No. 38,072